13:36:24 OCA PAD INITIATION - PROJECT HEADER INFORMATION 07/26/90

Active

Project #: E-16-M06 Cost share #: Rev #: 0
Center # : 10/24-6-R6572-2A1 Center shr #: OCA file #:
Work type : RES
Contract#: LTD DTD 7/6/90 Mod #: Document : SUBCONT
Prime #: 5 R01 HL41267-03 Contract entity: GTRC

Subprojects ? : N
Main project #:

Project unit: AERO ENGR Unit code: 02.010.110
Project director(s):
GIDDENS D P AERO ENGR (404)894-3781

Sponsor/division names: UNIV OF CHICAGO / CHICAGO, IL
Sponsor/division codes: 400 / 015

Award period: 900501 to 910430 (performance) 910630 (reports)

Sponsor amount	New this change	Total to date
Contract value	110,221.00	110,221.00
Funded	110,221.00	110,221.00
Cost sharing amount		0.00

Does subcontracting plan apply ?: N

Title: BIOMECHANICAL FACTORS IN ANASTOMOTIC INTIMAL HYPERPLASIA

PROJECT ADMINISTRATION DATA

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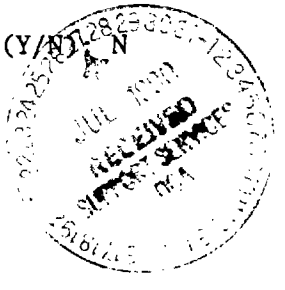
Security class (U,C,S,TS) : U ONR resident rep. is ACO (Y/N): N
Defense priority rating : N/A NIH supplemental sheet
Equipment title vests with: Sponsor GIT X

Administrative comments -
INITIATION OF PROJECT. CONTINUATION OF E-16-A17.



GEORGIA INSTITUTE OF TECHNOLOGY
OFFICE OF CONTRACT ADMINISTRATION

NOTICE OF PROJECT CLOSEOUT

Closeout Notice Date 07/02/91

Project No. E-16-M06_____ Center No. 10/24-6-R6572-2A1_

Project Director GIDDENS D P_____ School/Lab AERO ENGR_____

Sponsor UNIV OF CHICAGO/CHICAGO, IL_____

Contract/Grant No. LTD DTD 7/6/90_____ Contract Entity GTRC

Prime Contract No. 5 R01 HL41267-03_____

Title BIOMECHANICAL FACTORS IN ANASTOMOTIC INTIMAL HYPERPLASIA_____

Effective Completion Date 910430 (Performance) 910630 (Reports)

Closeout Actions Required:	Y/N	Date Submitted
Final Invoice or Copy of Final Invoice	Y	910405
Final Report of Inventions and/or Subcontracts	Y	_____
Government Property Inventory & Related Certificate	N	_____
Classified Material Certificate	N	_____
Release and Assignment	N	_____
Other _____	N	_____

Comments_____

_____

Subproject Under Main Project No. _____

Continues Project No. E-16-A17_____

Distribution Required:

Project Director	Y
Administrative Network Representative	Y
GTRI Accounting/Grants and Contracts	Y
Procurement/Supply Services	Y
Research Property Managment	Y
Research Security Services	N
Reports Coordinator (OCA)	Y
GTRC	Y
Project File	Y
Other _____	N
_____	N

NOTE: Final Patent Questionnaire sent to PDPI.

BIOMECHANICAL FACTORS IN ANASTOMOTIC INTIMAL HYPERPLASIA

Technical Progress Report
Principal Investigator - Christopher K. Zarins, MD
Grant No. 5 RO1 HL41267-04
The University of Chicago
5/1/90-4/30/91

Rationale

It is our working hypothesis that the distribution of anastomotic intimal hyperplasia at vascular graft anastomoses corresponds to the distribution of shear stress acting on the wall at the fluid wall interface and occurs principally in regions of lowered and oscillatory shear stress. To test this hypothesis we have constructed vascular bypass grafts in dogs under conditions of differing anastomotic geometry, flow conditions and wall characteristics to precisely document the localization of anastomotic intimal thickening. This grant is a collaborative project with the Georgia Institute of Technology (Dr. Don P. Giddens) where analogous models are fashioned for precise quantitative documentation of the flow field. Correlative studies between in vivo observations on vascular anastomoses and in vitro characterization of the flow field will allow precise definition of the role of hemodynamic factors in anastomotic intimal hyperplasia.

Summary of Accomplishments

1. Intimal thickening vs. Intimal Hyperplasia. Significant differences exist between anastomotic intimal thickening which may be a feature of the normal healing response and anastomotic intimal hyperplasia which results in lumen narrowing. The precise factors which determine the development of one or the other are not known but histologically and functionally the two are distinguishable. Precise and differentiation between these two types of intimal hyperplasia are necessary for experimental and clinical studies. These concepts and differences were published in the Journal of Vascular Surgery in November of 1989, "Is Intimal Hyperplasia an Adaptive Response of a Pathologic Process/Observations on the Nature of Nonatherosclerotic Intimal Thickening", Seymour Glagov and Christopher K. Zarins.

2. All anastomotic intimal thickening is not the same. Investigation of anastomotic intimal thickening experimental saphenous vein and PTFE iliofemoral bypass grafts in dogs has revealed two separate and distinct kinds of intimal thickening. One is along the suture line and is increased in PTFE anastomoses suggesting that compliance mismatch may be a factor. The second type of intimal thickening occurs away from the suture line and on the floor of the recipient artery. This is in an area of flow oscillation and may be hemodynamically induced. This type of intimal thickening is the same in both vein and PTFE bypasses. This information has been presented and published at the Cardiovascular Science and Technology Meeting in Louisville, Kentucky December 1, 1990, "Anastomotic Intimal Thickening in End to Side Arterial Anastomoses", HS Bassiouny, S White, CK Zarins, DP Giddens and S Glagov. Further quantitative assessment of this phenomenon has been accepted for presentation at the Society for Vascular Surgery Meeting in Boston in June of 1991 and will be published in the future in the Journal of Vascular Surgery.

3. Hemodynamic characterization of end-to-side vascular anastomoses. Precise models of end-to-side anastomoses fashioned from castings of actual in vivo canine anastomoses have been performed at the Georgia Institute of Technology. Flow behavior has been studied under study in pulsatile flow conditions. Reynolds number divisions of flow in the outflow tracts in the pulsatile weigh form employed were taken from measurements obtained in the canine models. Flow visualization at the anastomoses revealed strong three dimensional helical patterns which formed in the anastomotic junction. Regions of low wall shear stress oscillatory wall shear and long particle residence times were identified from the flow

visualization experiments. A manuscript on these findings is currently under consideration by the Journal of Biomechanical Engineering, "Hemodynamic Patterns in a Model of End-to-Side Vascular Graft Anastomoses: Effects of Pulsatility, Flow Division and Reynolds Number", SS White, CK Zarins, H Bassiouny, F Loth, S Glagov and DP Giddens. The effects of altering anastomotic geometry with four to one and eight to one length to vessel diameter ratios and its effects on flow patterns was presented and published at the Cardiovascular Science and Technology Meeting in Louisville, Kentucky December 2, 1989, "Flow Patterns and Models of End-to-Side Vascular Grafts", DP Giddens, SS White, CK Zarins, H Bassiouny and S Glagov.

4. Exercise flow conditions eliminate stasis at vascular graft anastomosis. Modifications in the flow field due to exercise are of particular importance in lower extremity vascular graft anastomoses because a very large fluctuations in flow are experienced. In vivo. In an effort to determine the effect of exercise in vascular anastomotic hemodynamics was studied in a model vascular anastomosis. Exercise flow conditions were simulated by increasing both heart rate and flow. Areas of particle stasis and accumulation which were present at rest were rapidly eliminated under exercise flow conditions. The strength of the separation vortices during peak systole were significantly enhanced during exercise and strong helical and secondary flow patterns appeared which resulted in rapid particle clearance and elimination of stasis at the anastomoses. If prolonged particle residence times are a significant feature in an anastomotic intimal hyperplasia then this could be ameliorated with exercise. These findings were published in "Exercise Flow Conditions Eliminate Stasis at Vascular Graft Anastomoses", EM Giddens, DP Giddens, SS White, CK Zarins, HS Bassiouny and S. Glagov; in Biofluid Mechanics 3, ed. DJ Schenck and CL Lucas. New York Ohio Press, NY pp. 255-267, 1990. The relationship between anastomotic hemodynamics and the intimal thickening was further discussed at the Research Initiatives in Vascular Disease Meeting in February of 1991 in Bethesda, Maryland and submitted for publication under the title, "Relationship Between Anastomotic Hemodynamics and Intimal Thickening", CK Zarins and DP Giddens. This will appear in the Journal of Vascular Surgery in the near future.

5. The hemodynamic conditions of vascular anastomoses may lead to significant problems not only in lower extremity bypasses but in graft to vein anastomoses for vascular access. The hemodynamic considerations in intimal hyperplasia under these conditions was published in "Vascular Access for Hemodialysis II, Bruce G. Sommer and Mitchell L. Henry, editors, "Hemodynamic Effects and Tissue Reactions at Grant to Vein Anastomosis for Vascular Access", S Glagov, DP Giddens, HS Bassiouny, S White and CK Zarins, p. 3-20, 1990.

Current Investigations

No significant problems have developed and work is proceeding as outlined in the original grant proposal. We have developed a system for developing wall stress across the anastomoses using computerized particle tracking (Dr. Ray Vito). Preliminary work suggests that this will be a favorable technique and will allow quantitative assessment of in vivo compliance characteristics of these anastomoses.

Plans for the Coming Year

We will continue work as outlined in our original grant proposal. Particular attention is being paid to quantitative three-dimensional reconstruction of anastomotic thickening and quantitative laser doppler anemometry measurements of the anastomotic flow field in model flow circumstances. With these quantitative data correlations will be able to be performed in the future.

Publications

1. Is intimal hyperplasia an adaptive response or a pathologic process? - observations on the nature of nonatherosclerotic intimal thickening. S Glagov and CK Zarins. Special Communication 10:5, 571-573, 1989.

2. Flow patterns in models of end-to-side vascular grafts. DP Giddens, S White, CK Zarins, HS Bassiouny and S Glagov. Card Sci & Tech 1-2, 1989.

3. Anastomotic intimal thickening in end to side arterial anastomoses. HS Bassiouny, S White, CK Zarins, DP Giddens and S. Glagov. Card Sci & Tech 2-3, 1990.

4. Hemodynamic patterns in a model of end-to-side vascular graft anastomoses: effects of pulsatility, flow division and reynolds number. SS White, CK Zarins, HS Bassiouny, F. Loth, S Glagov and DP Giddens. J Biomech Eng 1990.

5. Hemodynamic effects and tissue reactions at graft to vein anastomosis for vascular access. S Glagov, DP Giddens, HS Bassiouny, S White and CK Zarins. Vasc Acc for Hemo-II 3-20, 1991.

6. Exercise flow conditions eliminate stasis at vascular graft anastomoses. EM Giddens, DP Giddens, SS White, CK Zarins, HS Bassiouny and S Glagov. Y-P Chen & RE Mates 254-267, 1991.

Reprints

See attached copies.

PROGRAM INCOME

There is no anticipated program income from this award.